Critical Care Medicine
August 2025 • Volume 53 • Number 8 • Pages e1620–e1629

CLINICAL INVESTIGATION

Lactate Values and Mortality in Patients With Cardiogenic Shock: Insights From the Altshock-2 Registry

OBJECTIVES: We aimed to evaluate the prognostic role of baseline and 24-hour plasma lactates in patients with cardiogenic shock (CS).

DESIGN: Multicenter, observational, prospective Altshock-2 Registry (NCT04295252) enrolling patients with CS since March 2020.

SETTING: Multicenter Italian Registry (12 centers).

PATIENTS: Six hundred fifty-one consecutive patients with CS and available data on lactate values.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: The association of baseline and 24-hour lactates with in-hospital mortality (primary endpoint) was evaluated. The optimal lactate cutoff points for predicting outcomes were identified in the overall cohort and among patients treated with mechanical circulatory support (MCS). Among the 651 included patients with CS, the mean age was 64 ± 14 years and 76% were male. On admission, patients with lactates less than 2.0, 2.1–4.0, and greater than 4.0 mmol/L were 248 (38.1%), 172 (26.4%), and 231 (35.5%), respectively. An improvement in lactate values at 24 hours was observed in 76.5% of patients. Baseline and 24-hour lactates were both independently associated with increased mortality (adjusted odds ratios for each 1-mmol/L increase: 1.08 [95% CI, 1.02–1.14] for baseline lactate; and 1.37 [95% CI, 1.15–1.63] for 24-hr lactate), but 24-hour lactates had a higher predictive accuracy than baseline lactates (area under the curve 0.702 vs. 0.648). The optimal baseline and 24-hour lactate cutoffs for predicting mortality were 3.2 mmol/L and 1.7 mmol/L, respectively, and varied in patients treated with MCS at different time points.

CONCLUSIONS: Higher baseline and 24-hour lactates were both independently associated with increased in-hospital mortality in patients with CS, although the 24-hour value had a higher predictive accuracy. Optimal lactate cutoffs for predicting mortality varied between admission and 24 hours and according to the MCS strategies.

KEYWORDS: cardiogenic shock; lactate; mechanical circulatory support; mortality; outcomes

Matteo Pagnesi, MD, PhD[1]
Mauro Riccardi, MD[1]
Alice Sacco, MD[2]
Giovanna Viola, MD[2]
Fabrizio Oliva, MD[2]
Simone Frea, MD[3]
Martina Briani, MD[4]
Letizia Fausta Bertoldi, MD[4]
Maurizio Bertaina, MD[5]
Luciano Potena, MD, PhD[6]
Serafina Valente, MD[7]
Marco Marini, MD[8]
Gaetano Maria De Ferrari, MD[3]
Nicoletta D'Ettore, MD[9]
Astrid Cardinale, MD[10]
Rita Camporotondo, MD[11]
Matteo Rota, PhD[12]
Guido Tavazzi, MD[13]
Nuccia Morici, MD, PhD[14]
Federico Pappalardo, MD[15,16]
Marco Metra, MD[1]
on behalf of the Altshock-2 Investigators

Cardiogenic shock (CS) constitutes a life-threatening condition of multiorgan hypoperfusion due to impaired cardiac output caused by primary cardiac dysfunction (1). High levels of lactate in this setting are a marker for hypoperfusion as insufficient oxygen supply to tissues leads to anaerobic metabolism, causing the accumulation of lactate (2). For this reason, the role of baseline lactate in CS is well established both from a diagnostic and prognostic point of view (3–7). Lactate levels, however, are not static over time.

Copyright © 2025 by the Society of Critical Care Medicine and Wolters Kluwer Health, Inc. All Rights Reserved.

DOI: 10.1097/CCM.0000000000006738

Copyright © 2025 by the Society of Critical Care Medicine and Wolters Kluwer Health, Inc. All Rights Reserved.

SHOUT
SHARE
IT

KEY POINTS

Question: What is the prognostic value of baseline and 24-hour lactate value in cardiogenic shock (CS)? Which are the optimal lactate cutoffs for predicting in-hospital mortality?

Findings: In patients with CS, higher baseline and 24-hour lactates were both independently associated with increased in-hospital mortality, although the 24-hour value had a higher predictive accuracy. Different optimal lactate cutoffs for predicting mortality were identified on admission and at 24 hours, and also varied according to the mechanical circulatory support (MCS) strategies.

Meaning: Both baseline and 24-hour lactates are prognostic in patients with CS, although 24-hour lactate reassessment may be more useful to identify patients at increased risk of mortality. Lactate values and changes need to be contextualized according to the MCS settings since different cutoffs were identified on admission and at 24 hours and according to the MCS strategies.

It was therefore shown that temporal lactate trends, particularly lactate clearance in the first 24 hours after CS onset, could have greater prognostic accuracy compared with baseline assessment alone, potentially providing a therapeutic target for guiding and updating clinical decisions in real time (8–11). In addition, short-term mechanical circulatory support (MCS) is increasingly used in patients with CS (12–16). Early lactate reassessment might be particularly important to inform clinical decision-making among patients treated with MCS as upfront or rescue therapy.

The aim of the present study was to evaluate the prognostic role of baseline and 24-hour lactate values in a large real-world multicenter cohort of patients with CS and to explore the optimal lactate cutoffs for predicting mortality in different settings, including patients treated with temporary MCS.

METHODS

Study Design

The Altshock-2 Registry (NCT04295252) is a multicenter, prospective, observational registry enrolling consecutive patients admitted for CS at 12 Italian centers since March 2020 (17–19). CS was defined and staged according to the Society for Cardiovascular Angiography and Interventions (SCAI) criteria (19, 20). In accordance with the European Union Regulation 536/2014, all competent patients provided written informed consent, whereas consent was waived for patients who were not competent on admission. The study was conducted in accordance with ethical principles based on the Declaration of Helsinki (21), the International Conference on Harmonization for Good Clinical Practice, and the current ethical rules. This study was first approved by the local Ethics Committee "Milano Area 3" of the ASST Grande Ospedale Metropolitano Niguarda (Piazza Ospedale Maggiore 3, 20162, Milan, Italy) on February 12, 2020 (study title "Cardiogenic shock: a prospective national registry to get insights in patients' profile, management and outcome_Registro Altshock-2"). The Strengthening the Reporting of Observational Studies in Epidemiology Guidelines was followed for reporting study findings (22).

Only patients with known baseline lactate values were considered for the present analysis. For this analysis, patients were divided into three groups according to lactate values sampled at baseline and 24 hours: 1) lactate values less than or equal to 2.0 mmol/L, 2) lactate values between 2.1 and 4.0 mmol/L, and 3) lactate values greater than 4.0 mmol/L.

Patients' characteristics, in-hospital data, and clinical outcomes of all consecutively enrolled patients were collected and registered in an electronic case report form through the RedCap platform. Data on vital parameters, laboratory findings, echocardiographic findings, and details on therapeutic management, as well as the SCAI shock stages according to the updated classification, were also reported (20).

The outcome of interest of this study was in-hospital mortality.

Statistical Analysis

Continuous variables are presented as mean ± SD or median and interquartile range (IQR), as appropriate, and were compared with analysis of variance or Kruskal-Wallis test, respectively. Categorical variables are presented as numbers and percentages and were compared with the χ^2 test. Sankey diagram was used

Copyright © 2025 by the Society of Critical Care Medicine and Wolters Kluwer Health, Inc. All Rights Reserved.

to show the distribution and flow of patients across the lactate categories from baseline to 24 hours. Baseline characteristics, in-hospital data, hemodynamic parameters, and in-hospital mortality were compared among the three groups based on lactate values at baseline and at 24 hours. Violin plots were used to show the distribution and density of baseline and 24-hour lactate values, respectively, among patients with in-hospital survival vs. in-hospital death.

Univariable and multivariable binary logistic regression analyses were performed to evaluate the impact of baseline and 24-hour lactate values on in-hospital mortality. The impact of lactates as a continuous variable and as a three-category variable (≤ 2.0 mmol/L vs. 2.1–4.0 mmol/L vs. > 4.0 mmol/L) was evaluated. The following clinically relevant variables in the context of CS were included in the multivariable analyses: age, sex, CS etiology, cardiac arrest at presentation, mean arterial pressure (MAP), estimated glomerular filtration rate (eGFR), need for MCS and SCAI classification. Results of logistic regression analyses are reported as unadjusted or adjusted odds ratio (OR) with a 95% CI. The performance of baseline and 24-hour lactate levels in predicting in-hospital mortality was evaluated in terms of discrimination by using the area under the curve (AUC) of the receiver operating characteristic curves. The Youden index was used to identify the optimal lactate cutoffs for predicting in-hospital mortality in the overall cohort and in the subgroups of patients treated with "upfront" MCS (i.e., on admission), "early" MCS (i.e., after admission but within 24 hr) and "late" MCS (i.e., after 24 hr).

Analyses were performed with STATA software version 16 (StataCorp., College Station, TX). A p value of less than 0.05 was considered statistically significant.

RESULTS

Baseline Characteristics and Clinical Presentation

A total of 651 patients with CS were included in the present study. Overall mean age was 64 ± 14years, 76% of patients were male and the baseline median lactate value was 2.7 mmol/L (IQR 1.6–5.8 mmol/L) in the overall population. Baseline characteristics according to baseline lactate levels are reported in **Supplemental Table 1** (https://links.lww.com/CCM/H735). On admission, 248 (38.1%) patients had a lactate value of less than 2.0 mmol/L, 172 (26.4%) had a value of 2.1–4.0 mmol/L and 231 (35.5%) had a value of greater than 4.0 mmol/L. The most common etiology of CS was acute coronary syndrome (ACS) (49%), followed by heart failure (HF)-CS in 29% of patients (Supplemental Table 1, https://links.lww.com/CCM/H735). Patients with baseline lactate greater than 4.0 mmol/L had more frequent ACS-CS (55%) as compared with those with lower lactate values. Conversely, HF-CS was observed more commonly in patients with baseline lactate less than or equal to 2.0 mmol/L (p = 0.019). Cardiac arrest at presentation was observed in 41% of patients with lactate greater than 4.0 mmol/L and only in 15% of patients with lactate less than 2.0 mmol/L ($p < 0.001$). Regarding the SCAI stage on admission, most patients presented with SCAI stage C (52%), followed by stage D (24%). SCAI stages at 24 hours according to 24-hour lactate values are reported in **Supplemental Table 2** (https://links.lww.com/CCM/H735).

In-hospital data on admission according to baseline lactate values are reported in **Supplemental Table 3** (https://links.lww.com/CCM/H735). Regarding vital parameters, systolic blood pressure and MAP were significantly lower in patients with lactate greater than 4.0 mmol/L ($p < 0.001$ and $p = 0.001$, respectively). On admission, patients with lactate greater than 4.0 mmol/L had lower HCO_3- values and eGFR, and higher glycemia, liver enzymes, and *N*-terminal pro B-type natriuretic peptide concentrations. Regarding echocardiographic data, left ventricular ejection fraction was similar between groups, whereas tricuspid annular plane systolic excursion was lower in patients with baseline lactate greater than 4.0 mmol/L. In-hospital data measured at 24 hours according to 24-hour lactate values are reported in **Supplemental Table 4** (https://links.lww.com/CCM/H735).

Figure 1 shows the flow of patients across the three lactate categories from admission to 24 hours. Among 595 patients with data both at baseline and 24 hours, 455 (76.5%) patients had a decrease in lactate values between baseline and 24 hours, whereas 140 (23.5%) patients had unchanged or rising values. The median lactate value at 24 hours was 1.5 mmol/L (IQR 1.1–2.3 mmol/L) in the overall population.

In-Hospital Therapeutic Management

In-hospital management is described in **Supplemental Tables 5** and **6** (https://links.lww.com/CCM/H735). The maximum inotropic score was higher in patients

Copyright © 2025 by the Society of Critical Care Medicine and Wolters Kluwer Health, Inc. All Rights Reserved.

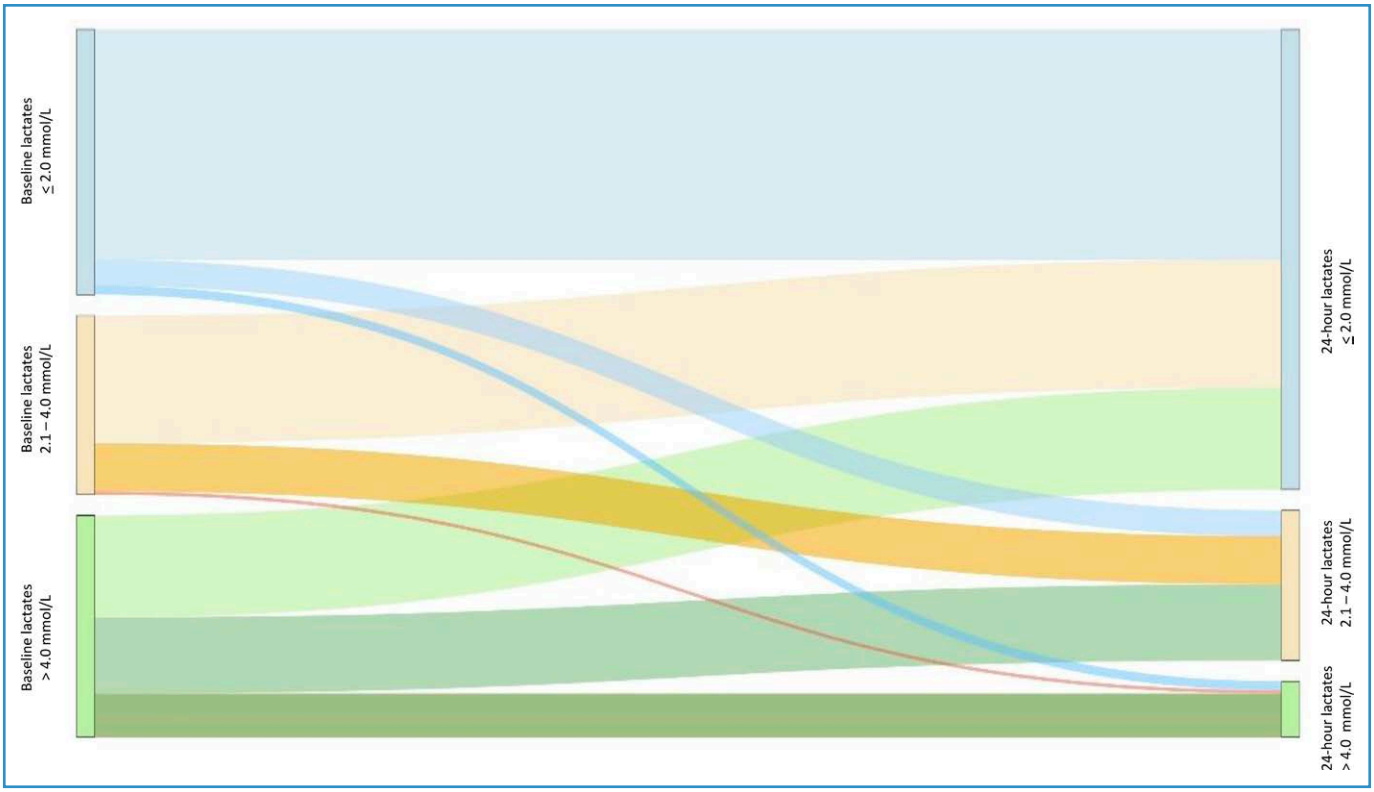
Baseline lactates ≤ 2.0 mmol/L
Baseline lactates 2.1 – 4.0 mmol/L
Baseline lactates > 4.0 mmol/L
24-hour lactates ≤ 2.0 mmol/L
24-hour lactates 2.1 – 4.0 mmol/L
24-hour lactates > 4.0 mmol/L

Figure 1. Distribution of lactates on admission and at 24 hr. The Sankey diagram shows the distribution and flow of patients across lactate categories from baseline (i.e., admission) to 24 hr.

with lactate values greater than 4.0 mmol/L ($p < 0.001$). Patients with baseline lactates greater than 4.0 mmol/L were treated more frequently with norepinephrine (73%) and epinephrine (71%) as compared with the other groups. Conversely, levosimendan and sodium nitroprusside were used more frequently in patients with baseline lactate values less than or equal to 2.0 mmol/L.

Short-term MCS devices were used in 65% of patients, with no significant differences overall in MCS use between the three groups (Supplemental Table 5, https://links.lww.com/CCM/H735). Overall, the intra-aortic balloon pump (IABP) was the most frequently used support (80%). Patients with lactate values greater than 4.0 mmol/L were more likely to be treated with Impella and veno-arterial extracorporeal membrane oxygenation ($p = 0.011$ and $p < 0.001$, respectively) and less likely to be treated with IABP ($p = 0.001$). Continuous renal replacement therapy and mechanical ventilation were used more frequently in patients with lactates greater than 4.0 mmol/L (both $p < 0.001$), whereas non-invasive ventilation was used more frequently in patients with lactates less than or equal to 2.0 mmol/L ($p < 0.001$).

Impact of Lactate Values on Mortality

Overall in-hospital mortality was 36.7% (38.3% in ACS-CS, 38.2% in HF-CS, and 31.4% in other etiologies). In-hospital mortality according to baseline and 24-hour lactate values is reported in **Figure 2**. Patients with baseline lactate values greater than 4.0 mmol/L had higher in-hospital mortality as compared with those with lactate values 2.1–4.0 mmol/L and less than or equal to 2.0 mmol/L (49% vs. 37% vs. 25%, $p < 0.001$). Similarly, patients with lactate values greater than 4.0 mmol/L at 24 hours had higher in-hospital mortality than those in the other two groups (65% vs. 50% vs. 25%, $p < 0.001$). At multivariable analysis (**Table 1**), baseline lactate was independently associated with increased in-hospital mortality, both when evaluated as a continuous variable (adjusted OR for each 1-mmol/L increase 1.08; 95% CI, 1.02–1.14; $p = 0.008$) and as a three-categories variable (adjusted OR for lactate > 4.0 mmol/L vs. ≤ 2.0 mmol/L 1.71; 95% CI, 1.01–2.89; $p = 0.047$; adjusted OR for lactate 2.1–4.0 mmol/L vs. ≤ 2.0 mmol/L 1.82; 95% CI, 1.06–3.13; $p = 0.029$). Lactate values at 24 hours were also independently associated with increased in-hospital death,

Copyright © 2025 by the Society of Critical Care Medicine and Wolters Kluwer Health, Inc. All Rights Reserved.

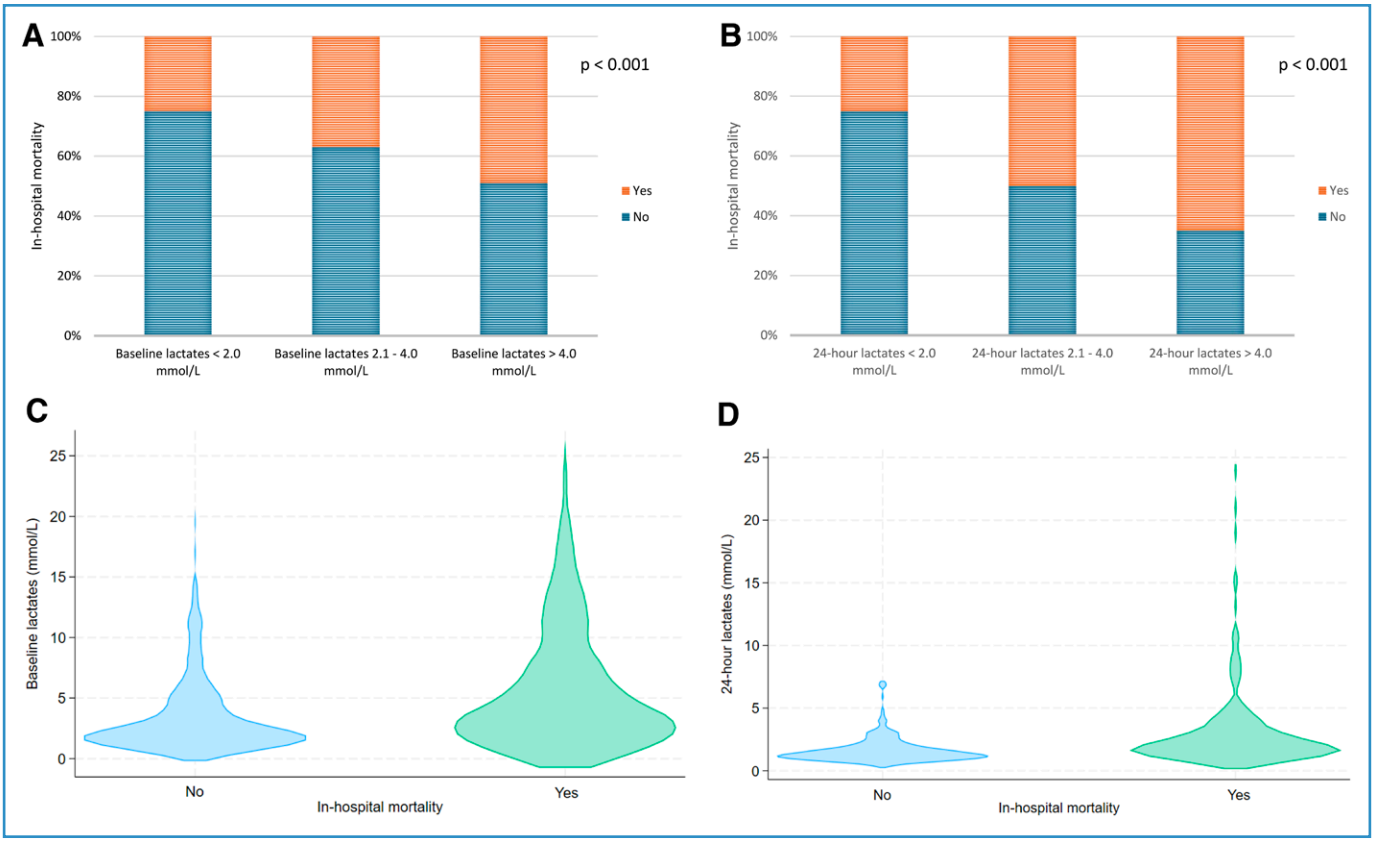

Figure 2. Lactate values and in-hospital mortality. In-hospital mortality is reported according to baseline (**A**) and 24-hr (**B**) lactate values. The *violin plots* show the distribution of baseline (**C**) and 24-hr (**D**) lactate values in patients with in-hospital survival or in-hospital death.

with higher ORs as compared with baseline lactates assessed both as a continuous variable (adjusted OR for each 1-mmol/L increase 1.37; 95% CI, 1.15–1.63; $p < 0.001$) and as a three-categories variable (adjusted OR for lactate > 4.0 mmol/L vs. ≤ 2.0 mmol/L 4.31; 95% CI, 1.82–10.16; $p = 0.001$; adjusted OR for lactate 2.1–4.0 mmol/L vs. ≤ 2.0 mmol/L 1.91; 95% CI, 1.12–3.25; $p = 0.018$). Lactate values at 24 hours showed a higher accuracy than baseline lactate values in predicting in-hospital mortality (AUC 0.702 vs. 0.648; **Fig. 3**).

An independent association between worsening or unchanged lactates at 24 hours and mortality was also observed (adjusted OR 1.81; 95% CI, 1.12–2.94; $p = 0.016$; Table 1). Among the patients who had an improvement in lactates, the amount of lactate reduction was significantly associated with lower mortality (crude OR for each 1-mmol/L change in lactates 0.92; 95% CI, 0.86–0.97; $p = 0.004$), whereas a nonsignificant trend toward higher mortality with increasing lactate values was observed among those who had worsening or unchanged lactates (crude OR for each 1-mmol/L lactate increase 1.21; 95% CI, 0.96–1.52; $p = 0.099$).

Optimal Lactate Cutoffs for Predicting Mortality

Table 2 reports the optimal lactate cutoff points for predicting in-hospital mortality. Overall, the optimal baseline lactate cutoff was 3.2 mmol/L (AUC 0.61), whereas the optimal 24-hour lactate cutoff was 1.7 mmol/L (AUC 0.67). Among patients treated with MCS on admission, the optimal lactate cutoff point at baseline was 5.3 mmol/L (AUC 0.66), whereas at 24 hours it was 1.8 mmol/L (AUC 0.72). Among patients treated with "early" MCS (i.e., after admission but within 24 hr), the optimal baseline lactate cutoff was 2.2 mmol/L (AUC 0.71), whereas the optimal 24-hour lactate cutoff was 2.1 mmol/L (AUC 0.65). Among patients who received a "late" MCS (i.e., after 24 hr), the optimal lactate cutoff point at baseline was 3.1 mmol/L (AUC 0.62), whereas at 24 hours it was 1.7 mmol/L (AUC 0.57).

DISCUSSION

This analysis of the large, observational, multicenter Altshock-2 Registry demonstrates that both baseline and 24-hour lactate levels are associated with

Copyright © 2025 by the Society of Critical Care Medicine and Wolters Kluwer Health, Inc. All Rights Reserved.

TABLE 1.
Impact of Baseline and 24-Hour Lactate Values on In-hospital Mortality

	Univariable Analysis		Multivariable Analysis	
Variable	**Unadjusted OR (95% CI)**	***p***	**Adjusted OR (95% CI)[a]**	***p***
Baseline lactates (admission)				
Lactates as a continuous variable (for each 1-mmol/L increase)	1.14 (1.09–1.19)	**< 0.001**	1.08 (1.02–1.14)	**0.008**
Lactate categories				
≤ 2.0 mmol/L	REF	REF	REF	REF
2.1–4 mmol/L	1.79 (1.16–2.76)	**0.009**	1.82 (1.06–3.13)	**0.029**
> 4 mmol/L	2.91 (1.96–4.32)	**< 0.001**	1.71 (1.01–2.89)	**0.047**
24-hr lactates				
Lactates as a continuous variable (for each 1-mmol/L increase)	1.55 (1.35–1.78)	**< 0.001**	1.37 (1.15–1.63)	**< 0.001**
Lactate categories				
≤ 2.0 mmol/L	REF	REF	REF	REF
2.1–4 mmol/L	3.12 (2.07–4.70)	**< 0.001**	1.91 (1.12–3.25)	**0.018**
> 4 mmol/L	5.78 (3.08–10.88)	**< 0.001**	4.31 (1.82–10.16)	**0.001**
Worsening or unchanged vs. improved lactates	1.58 (1.06–2.34)	**0.024**	1.81 (1.12–2.94)	**0.016**

OR = odds ratio, REF = reference category.
[a]Covariates included in the multivariable analysis are age, sex, causes of cardiogenic shock, cardiac arrest at presentation, need of mechanical circulatory support, mean arterial pressure at admission, estimated glomerular filtration rate at the time of admission, and Society for Cardiovascular Angiography and Interventions classification at the time of admission.
Data are presented as OR and 95% CI. Boldface values represent significant *p* values.

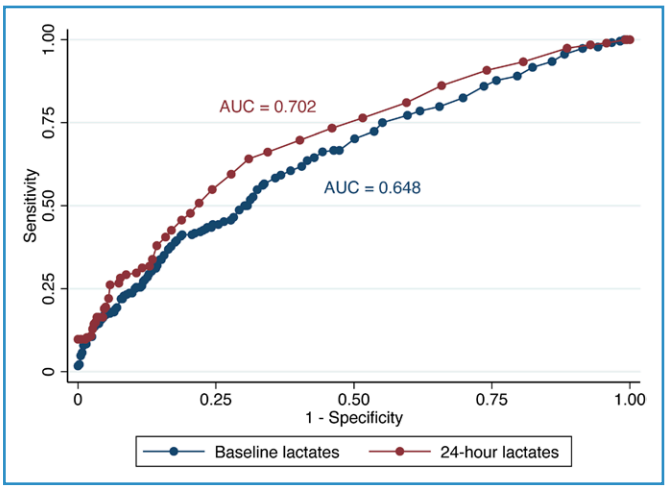

Figure 3. Predictive value of baseline and 24-hr lactate values. Receiver operating characteristic curve comparing the performance of baseline and 24-hr lactate levels in predicting in-hospital mortality. AUC = area under the curve.

in-hospital mortality among patients with CS. Lactate values at 24 hours have a higher accuracy in predicting mortality. Overall, optimal baseline and 24-hour lactate cutoffs for predicting in-hospital mortality were 3.2 mmol/L and 1.7 mmol/L, respectively, and the cutoffs varied depending on the timing of MCS use in patients treated with MCS.

Lactate Values on Admission in CS

Increased lactate levels are a sign of tissue hypoperfusion. Since point-of-care testing for arterial lactate in blood gas analysis has become widely available, this parameter has become widely used in clinical practice as a prognostic predictor of in-hospital and 30-day mortality (23, 24). An analysis of the CardShock Registry, a large European CS Registry, reported that lactates at the time of admission were a powerful predictor of 30-day mortality (adjusted hazard ratio 1.20; 95% CI, 1.14–1.27; $p < 0.001$) (25). Our analysis confirms the prognostic role of baseline lactate values, which were associated with increased in-hospital mortality both when evaluated as a continuous variable and as a

Copyright © 2025 by the Society of Critical Care Medicine and Wolters Kluwer Health, Inc. All Rights Reserved.

TABLE 2.
Optimal Lactate Cutoff Points to Predict In-Hospital Mortality in the Entire Cohort and Among the Patients Treated With Temporary Mechanical Circulatory Support

Cohorts	Optimal Cutoff Points (mmol/L)	AUC	Sensitivity	Specificity
Baseline lactates				
Overall (entire cohort), $n = 625$	3.2	0.61	0.57	0.66
MCS-treated cohort				
"Upfront" MCS[a], $n = 311$	5.3	0.66	0.53	0.79
"Early" MCS[b], $n = 43$	2.2	0.71	0.76	0.65
"Late" MCS[c], $n = 52$	3.1	0.62	0.43	0.81
24-hr lactates				
Overall (entire cohort), $n = 573$	1.7	0.67	0.64	0.69
MCS-treated cohort				
"Upfront" MCS[a], $n = 282$	1.8	0.72	0.74	0.71
"Early" MCS[b], $n = 42$	2.1	0.65	0.69	0.62
"Late" MCS[c], $n = 51$	1.7	0.57	0.41	0.72

AUC = area under the curve, MCS = mechanical circulatory support.
[a]Patients receiving MCS on admission.
[b]Patients receiving MCS after admission but within 24 hr.
[c]Patients receiving MCS after 24 hr.
Optimal cutoff points with the relative AUC, sensitivity, and specificity are reported (based on the Youden index).

three-categories variable with 2.0 mmol/L and 4.0 mmol/L cutoff values.

However, although baseline lactate values are often included in scores used for risk stratification of patients with CS, the optimal prognostic cutoff is not well known and varies between 2 mmol/L and 8 mmol/L according to previous studies (23, 26–28). For example, a lactate value greater than or equal to 5.0 mmol/L has been introduced as a prognostic parameter in the IABP in the Cardiogenic Shock II (IABP-SHOCK II) score for early risk stratification in CS (28). However, in a subsequent sub-analysis of the same study, a baseline lactate cutoff greater than or equal to 5.0 mmol/L was not significantly associated with 30-day mortality ($p = 0.60$) (24). In our analysis, the optimal baseline lactate cutoff value for the prediction of in-hospital mortality in the overall CS cohort resulted in 3.2 mmol/L. This threshold, which is much closer to the cutoff of 2 mmol/L currently used in the SCAI classification for identifying patients with overt CS, could better stratify patients with CS and be further validated in future studies focusing on risk stratification in CS.

The Importance of 24-Hour Reassessment

A reduction of lactate levels in the first 24 hours after CS onset is a marker of improved perfusion (restoration of tissue oxygen supply) and therefore must be a treatment goal as it is associated with better outcomes (2, 8, 10). In a meta-analysis of 12 studies that monitored lactate levels after CS onset, lactate clearance was significantly greater in survivors vs. non-survivors as early as 6 hours (21.9% vs. 0.6%) and this difference continued to increase up to at least 24 hours (60.7% vs. 40.3%) (9). Lactate trends up to 24 hours differed between survivors and non-survivors also in the National Cardiogenic Shock Initiative study enrolling patients with acute myocardial infarction-related CS (AMI-CS) treated with early MCS (Impella) (29). Our findings are in line with previous studies because of lack of lactate reduction within 24 hours was associated with an increased risk of in-hospital mortality.

In addition to the prognostic role of lactate clearance, the absolute lactate value measured at a reassessment during the first 24 hours has a prognostic role per se that seems even higher than the clearance

Copyright © 2025 by the Society of Critical Care Medicine and Wolters Kluwer Health, Inc. All Rights Reserved.

(25). Fuernau et al (24) reported that an 8-hour lactate reassessment was significantly better than the baseline value or lactate clearance during this time frame. Similarly, Klemm et al (11) showed that the 24-hour lactate level was the most effective predictor of 30-day mortality in CS, suggesting its superiority over baseline levels and lactate clearance. In our registry, 24-hour lactate values were not only independently associated with increased in-hospital mortality, but they showed higher accuracy than baseline lactate values in predicting in-hospital mortality. The optimal 24-hour lactate cutoff for predicting in-hospital mortality in the overall cohort was 1.7 mmol/L, lower than the 3.1 mmol/L cutoff reported in the IABP-SHOCK II sub-analysis (24).

These data confirm the importance of the 24-hour global reassessment of the CS patient, already shown in previous studies focused on SCAI staging, to improve risk stratification (19, 30).

Optimal Prognostic Cutoffs and Therapeutic Implications

Temporary MCS is a potential option to improve organ perfusion in patients with CS (31). However, despite the increased use of MCS in recent years, data from randomized trials in patients with AMI-CS are not uniformly encouraging (32–34). Beyond the DanGer Shock trial demonstrating a lower risk of death at 180 days among patients routinely treated with a microaxial flow pump as compared with standard care (35), the other trials on MCS were negative (32–34), partly attributable to the high risk of adverse events and device-related complications in patients treated with MCS devices (36, 37). Recently, in a large patient-level meta-analysis of randomized trials, the use of temporary MCS did not reduce 6-month mortality in patients with AMI-CS in the overall cohort, but only in the subset of patients with ST-elevation CS without risk of hypoxic brain injury, thus highlighting the importance of proper patient selection (38). However, the ideal criteria for candidacy to MCS and the optimal timing for starting and/or escalating MCS are still to be defined, and the individual patient's risk-benefit ratio should be considered to avoid futility.

In this context, early lactate reassessment may be particularly important to inform clinical decision-making among patients treated with temporary MCS as "upfront" or "rescue" therapy. In our study, among patients treated with "upfront" MCS, the optimal lactate cutoff point at baseline for predicting in-hospital mortality was 5.3 mmol/L, whereas it was 1.8 mmol/L at 24 hours, thus raising questions on the potential futility of placing MCS on admission or maintaining MCS (without escalation) at 24 hours in patients with lactate values above these thresholds. Of note, in the already mentioned patient-level meta-analysis of randomized trials, AMI-CS patients with baseline lactates greater than or equal to 5.0 mmol/L were those who gained the most benefit from active MCS as compared with controls (38). In the DanGer Shock trial, the median baseline lactate level was 4.5 mmol/L in the enrolled population, and the benefit of the microaxial flow pump vs. standard care seemed similar in patients with lactate less than or equal to 4.5 and in those with lactate greater than 4.5 mmol/L (35). In our study, the optimal lactate cutoff points at baseline and 24 hours were 2.2 mmol/L and 2.1 mmol/L, respectively, among patients treated with "rescue" MCS after admission but within 24 hours, thus indirectly confirming the lack of excess mortality in patients who received MCS in this time frame and had lactate values below these thresholds. However, our study was not specifically focused on evaluating the benefits of MCS based on lactate levels, but can only inform future trials properly testing different MCS strategies by suggesting potential lactate treatment goals. In addition to strategies for improving perfusion and oxygenation, recent evidence suggests that interventions targeting mitochondrial function may play a role in reducing organ damage under shock (39), and thus might be tested in patients with different lactate thresholds.

LIMITATIONS

Our study has some limitations. First, the present registry represents a real-world picture of the contemporary management of CS. However, patients were treated according to protocols that may vary between enrolling centers, thus potentially creating some bias in data collection and interpretation. Furthermore, some variables had a non-negligible number of missing values which could have influenced the study findings. For example, PAC was used in a minority of patients, and therefore invasive hemodynamic parameters were not available for most included patients and were not

Copyright © 2025 by the Society of Critical Care Medicine and Wolters Kluwer Health, Inc. All Rights Reserved.

analyzed. Finally, we cannot rule out that lactate values measured at other time points (e.g., after 1, 8, 12, or 48 hr) may be more accurate in predicting outcome than the investigated baseline and 24-hour values, thus resulting in higher AUC values.

CONCLUSIONS

In a contemporary, prospective, multicenter registry of patients with CS, higher baseline and 24-hour lactate levels were both independently associated with increased in-hospital mortality, although the 24-hour value had a higher accuracy in predicting this outcome. Optimal baseline and 24-hour lactate cutoffs for predicting mortality were 3.2 mmol/L and 1.7 mmol/L, respectively, in the overall cohort, and varied depending on the timing of MCS placement among patients treated with MCS. Future dedicated studies are needed to evaluate whether the decisions on MCS candidacy or escalation/de-escalation may be better informed by specific lactate cutoffs.

1 *Department of Medical and Surgical Specialties, Radiological Sciences and Public Health, Institute of Cardiology, University of Brescia, Spedali Civili di Brescia, Brescia, Italy.*

2 *Cardiac Intensive Care Unit, "De Gasperis" Cardio Center, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy.*

3 *Cardiac Intensive Care Unit, Città della Salute e della Scienza di Torino, Torino, Italy.*

4 *Cardiac Intensive Care Unit, Humanitas Research Hospital IRCCS Rozzano, Milan, Italy.*

5 *Division of Cardiology, San Giovanni Bosco Hospital, ASL Città di Torino, Torino, Italy.*

6 *Heart Failure and Transplant Unit, IRCCS Azienda Ospedaliero Universitaria di Bologna, Bologna, Italy.*

7 *Division of Cardiology, Department of Medical Biotechnologies, University of Siena, Siena, Italy.*

8 *Department of Cardiovascular Sciences, Clinic of Cardiology, Ospedali Riuniti, Ancona, Italy.*

9 *Division of Cardiology, Ospedale San Giacomo, Novi Ligure, Italy.*

10 *Department of Cardiothoracic and Vascular Anesthesia and Intensive Care, AOU SS Antonio e Biagio e Cesare Arrigo, Alessandria, Italy.*

11 *Cardiac Intensive Care Unit, Fondazione Policlinico San Matteo Hospital IRCCS, Pavia, Italy.*

12 *Units of Biostatistics and Biomathematics and Bioinformatics, Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy.*

13 *Department of Clinical-Surgical, Diagnostic and Paediatric Sciences, Unit of Anaesthesia and Intensive Care, University of Pavia Italy Anesthesia and Intensive Care, Fondazione Policlinico San Matteo Hospital IRCCS, Anestesia e Rianimazione I, Pavia, Italy.*

14 *IRCCS Fondazione Don Carlo Gnocchi, ONLUS, Milan, Italy.*

15 *"Kore" University, Enna, Italy.*

16 *Policlinico Centro Cuore G.B. Morgagni, Catania, Italy.*

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (https://journals.lww.com/ccmjournal).

Drs. Pagnesi, Sacco, Marini, and Metra received funding from AstraZeneca. Drs. Pagnesi and Metra received funding from Abbott Vascular, Boehringer Ingelheim, and Vifor Pharma. Dr. Pagnesi received funding from Novartis and Roche Diagnostics. Dr. Sacco received funding from Menarini. Drs. Viola and Marini received support for article research from the National Institutes of Health. Drs. Bertoldi, Marini, and Pappalardo received funding from Abiomed. Dr. Marini received funding from Orion. Dr. Metra received funding from Bayer, NovoNordisk, Actelion, Amgen, Edwards Therapeutics, Servier, and Windtree Therapeutics. The remaining authors have disclosed that they do not have any potential conflicts of interest.

For information regarding this article, E-mail: m.pagnesi@gmail.com

REFERENCES

1. Riccardi M, Pagnesi M, Chioncel O, et al: Medical therapy of cardiogenic shock: Contemporary use of inotropes and vasopressors. *Eur J Heart Fail* 2024; 26:411–431
2. Attanà P, Lazzeri C, Picariello C, et al: Lactate and lactate clearance in acute cardiac care patients. *Eur Heart J Acute Cardiovasc Care* 2012; 1:115–121
3. Valente S, Lazzeri C, Vecchio S, et al: Predictors of in-hospital mortality after percutaneous coronary intervention for cardiogenic shock. *Int J Cardiol* 2007; 114:176–182
4. Müllner M, Sterz F, Domanovits H, et al: The association between blood lactate concentration on admission, duration of cardiac arrest, and functional neurological recovery in patients resuscitated from ventricular fibrillation. *Intensive Care Med* 1997; 23:1138–1143
5. Weil MH, Afifi AA: Experimental and clinical studies on lactate and pyruvate as indicators of the severity of acute circulatory failure (shock). *Circulation* 1970; 41:989–1001
6. Cady LD, Weil MH, Afifi AA, et al: Quantitation of severity of critical illness with special reference to blood lactate. *Crit Care Med* 1973; 1:75–80
7. Weil MH, Ruiz CE, Michaels S, et al: Acid-base determinants of survival after cardiopulmonary resuscitation. *Crit Care Med* 1985; 13:888–892
8. Park IH, Yang JH, Jang WJ, et al: Clinical significance of lactate clearance in patients with cardiogenic shock: Results from the RESCUE registry. *J Intensive Care* 2021; 9:63
9. Marbach JA, Stone S, Schwartz B, et al: Lactate clearance is associated with improved survival in cardiogenic shock: A systematic review and meta-analysis of prognostic factor studies. *J Card Fail* 2021; 27:1082–1089

Copyright © 2025 by the Society of Critical Care Medicine and Wolters Kluwer Health, Inc. All Rights Reserved.

10. Marbach JA, Di Santo P, Kapur NK, et al: Lactate clearance as a surrogate for mortality in cardiogenic shock: Insights from the DOREMI trial. *J Am Heart Assoc* 2022; 11:e023322
11. Klemm G, Markart S, Hermann A, et al: Lactate as a predictor of 30-day mortality in cardiogenic shock. *J Clin Med* 2024; 13:1932
12. Malik A, Basu T, VanAken G, et al: National trends for temporary mechanical circulatory support utilization in patients with cardiogenic shock from decompensated chronic heart failure: Incidence, predictors, outcomes, and cost. *J Soc Cardiovasc Angiogr Interv* 2023; 2:101177
13. Nishimoto Y, Ohbe H, Matsui H, et al: Trends in mechanical circulatory support use and outcomes of patients with cardiogenic shock in Japan, 2010 to 2020 (from a Nationwide Inpatient Database Study). *Am J Cardiol* 2023; 203:203–211
14. Shah M, Patnaik S, Patel B, et al: Trends in mechanical circulatory support use and hospital mortality among patients with acute myocardial infarction and non-infarction related cardiogenic shock in the United States. *Clin Res Cardiol* 2018; 107:287–303
15. Vallabhajosyula S, Prasad A, Sandhu GS, et al; Colaborators: Ten-year trends, predictors and outcomes of mechanical circulatory support in percutaneous coronary intervention for acute myocardial infarction with cardiogenic shock. *EuroIntervention* 2021; 16:e1254–e1261
16. Salter BS, Gross CR, Weiner MM, et al: Temporary mechanical circulatory support devices: Practical considerations for all stakeholders. *Nat Rev Cardiol* 2023; 20:263–277
17. Sacco A, Montisci A, Tavecchia G, et al; on behalf of AltShock-2 Investigators: Ventilation strategies in cardiogenic shock: Insights from the AltShock-2 registry. *Eur J Heart Fail* 2024; 26:2412–2420
18. Bertaina M, Morici N, Frea S, et al: Differences between cardiogenic shock related to acute decompensated heart failure and acute myocardial infarction. *ESC Heart Fail* 2023; 10:3472–3482
19. Morici N, Frea S, Bertaina M, et al: SCAI stage reclassification at 24 h predicts outcome of cardiogenic shock: Insights from the Altshock-2 registry. *Catheter Cardiovasc Interv* 2023; 101:22–32
20. Naidu SS, Baran DA, Jentzer JC, et al: SCAI SHOCK stage classification expert consensus update: A review and incorporation of validation studies. *J Am Coll Cardiol* 2022; 79:933–946
21. World Medical Assocation: World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA* 2013; 310:2191–2194
22. Vandenbroucke JP, von Elm E, Altman DG, et al; STROBE Initiative: Strengthening the reporting of observational studies in epidemiology (STROBE): Explanation and elaboration. *PLoS Med* 2007; 4:e297
23. Harjola V-P, Lassus J, Sionis A, et al; CardShock Study Investigators: Clinical picture and risk prediction of short-term mortality in cardiogenic shock. *Eur J Heart Fail* 2015; 17:501–509
24. Fuernau G, Desch S, de Waha-Thiele S, et al: Arterial lactate in cardiogenic shock: Prognostic value of clearance versus single values. *JACC Cardiovasc Interv* 2020; 13:2208–2216
25. Lindholm MG, Hongisto M, Lassus J, et al: Serum lactate and a relative change in lactate as predictors of mortality in patients with cardiogenic shock—results from the cardshock study. *Shock* 2020; 53:43–49
26. Beer BN, Jentzer JC, Weimann J, et al: Early risk stratification in patients with cardiogenic shock irrespective of the underlying cause—the Cardiogenic Shock Score. *Eur J Heart Fail* 2022; 24:657–667
27. Muller G, Flecher E, Lebreton G, et al: The ENCOURAGE mortality risk score and analysis of long-term outcomes after VA-ECMO for acute myocardial infarction with cardiogenic shock. *Intensive Care Med* 2016; 42:370–378
28. Pöss J, Köster J, Fuernau G, et al: Risk stratification for patients in cardiogenic shock after acute myocardial infarction. *J Am Coll Cardiol* 2017; 69:1913–1920
29. Basir MB, Lemor A, Gorgis S, et al: Early utilization of mechanical circulatory support in acute myocardial infarction complicated by cardiogenic shock: The national cardiogenic shock initiative. *J Am Heart Assoc* 2023; 12:e031401
30. Ton V-K, Li S, John K, et al: Serial shock severity assessment within 72 hours after diagnosis: A Cardiogenic Shock Working Group report. *J Am Coll Cardiol* 2024; 84:978–990
31. Combes A, Price S, Slutsky AS, et al: Temporary circulatory support for cardiogenic shock. *Lancet* 2020; 396:199–212
32. Thiele H, Zeymer U, Neumann F-J, et al; IABP-SHOCK II Trial Investigators: Intraaortic balloon support for myocardial infarction with cardiogenic shock. *N Engl J Med* 2012; 367:1287–1296
33. Thiele H, Zeymer U, Akin I, et al; ECLS-SHOCK Investigators: Extracorporeal life support in infarct-related cardiogenic shock. *N Engl J Med* 2023; 389:1286–1297
34. Ostadal P, Rokyta R, Karasek J, et al; ECMO-CS Investigators: Extracorporeal membrane oxygenation in the therapy of cardiogenic shock: Results of the ECMO-CS randomized clinical trial. *Circulation* 2023; 147:454–464
35. Møller JE, Engstrøm T, Jensen LO, et al; DanGer Shock Investigators: Microaxial flow pump or standard care in infarct-related cardiogenic shock. *N Engl J Med* 2024; 390:1382–1393
36. Bogerd M, Ten Berg S, Peters EJ, et al: Impella and venoarterial extracorporeal membrane oxygenation in cardiogenic shock complicating acute myocardial infarction. *Eur J Heart Fail* 2023; 25:2021–2031
37. Ancona MB, Montorfano M, Masiero G, et al: Device-related complications after Impella mechanical circulatory support implantation: An IMP-IT observational multicentre registry substudy. *Eur Heart J Acute Cardiovasc Care* 2021; 10:999–1006
38. Thiele H, Møller JE, Henriques JPS, et al: Temporary mechanical circulatory support in infarct-related cardiogenic shock: An individual patient data meta-analysis of randomised trials with 6-month follow-up. *Lancet* 2024; 404:1019–1028
39. de Carvalho LRP, Abreu SC, de Castro LL, et al: Mitochondria-rich fraction isolated from mesenchymal stromal cells reduces lung and distal organ injury in experimental sepsis. *Crit Care Med* 2021; 49:e880–e890

Copyright © 2025 by the Society of Critical Care Medicine and Wolters Kluwer Health, Inc. All Rights Reserved.